

**Synthesis of (-)-TAN-2483A. Revision of the Structures of and
Syntheses of (±)-FD-211 (Waal A) and (±)-FD-212 (Waal B)**

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Supporting Material

General Procedures. NMR spectra were recorded at 400 MHz in CDCl₃ unless otherwise indicated. Chemical shifts are reported in δ , coupling constants in Hz, and IR spectra in cm⁻¹.

(3*S*,4*S*)-Dihydro-4-hydroxy-3-(1*R*-hydroxyhexa-2*E*,4*E*-dienyl)-furan-2-one (9a) and (3*S*,4*S*)-Dihydro-4-hydroxy-3-(1*S*-hydroxyhexa-2*E*,4*E*-dienyl)-furan-2-one (12a). Lithium diisopropylamide was prepared from diisopropylamine (590 μ L, 4.2 mmol) and *n*-BuLi (1.5 mL, 2.8 M in hexane, 4.2 mmol) in THF (8 mL) at 0 °C. This solution was cooled to -78 °C and treated with (4*S*)-dihydro-4-hydroxyfuran-2-one (**10a**) (204 mg, 2 mmol) in THF (1 mL). The solution was stirred for 15 min at -78 °C and treated with a 4:1 mixture of (2*E*,4*E*)- and (2*E*,4*Z*)-2,4-hexadienal (**11**) (220 μ L, 2 mmol) in dry THF (1 mL). The mixture was warmed to -42 °C, stirred for 1 h, and quenched with saturated aqueous NH₄Cl solution (1 mL). The resulting mixture was diluted with ether (120 mL), washed with brine, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (3:1 hexanes/EtOAc) gave **12a** (150 mg, 38%) as a colorless oil, followed by **9a** (131 mg, 33%) as a colorless oil. Both of these compounds are a 4:1 mixture of (2*E*,4*E*) and (2*E*,4*Z*) isomers. Flash chromatography of the mixture of **9a** isomers on 20% AgNO₃ on silica gel (2:1 hexanes/EtOAc) gave (2*E*,4*E*)-**9a** (102 mg, 26%). Similar chromatography of the mixture of **12a** isomers gave (2*E*,4*E*)-**12a** (115 mg, 29%).

Data for **9a**: ¹H NMR 6.29 (dd, 1, *J* = 15.3, 10.4), 6.06 (ddq, 1, *J* = 15.3, 10.4, 1.2), 5.79 (dq, 1, *J* = 15.3, 6.7), 5.66 (dd, 1, *J* = 15.3, 7.3), 4.52-4.59 (m, 2), 4.45 (dd, 1, *J* = 9.8, 6.7), 4.09 (dd, 1, *J* = 9.8, 5.5), 3.56 (d, 1, *J* = 4.3, OH), 3.39 (d, 1, *J* = 3.1, OH), 2.79 (dd, 1, *J* = 5.5, 5.5),

1.77 (dd, 3, $J = 6.7, 1.2$); ^{13}C NMR 176.0, 133.7, 132.2, 130.1, 127.4, 73.3, 71.2, 69.4, 54.3, 18.2; IR (neat) 3359, 1762, 1662.

Data for **12a**: ^1H NMR 6.33 (dd, 1, $J = 15.3, 10.4$), 6.07 (ddq, 1, $J = 15.3, 10.4, 1.2$), 5.77 (dq, 1, $J = 15.3, 6.7$), 5.65 (dd, 1, $J = 15.3, 6.1$), 4.63-4.70 (m, 2), 4.46 (dd, 1, $J = 9.2, 4.6$), 4.09 (dd, 1, $J = 9.2, 6.1$), 3.18 (d, 1, $J = 4.9, \text{OH}$), 2.98 (d, 1, $J = 4.9, \text{OH}$), 2.68 (dd, 1, $J = 4.3, 4.3$), 1.77 (br d, 3, $J = 6.7$); ^{13}C NMR 177.1, 132.4, 131.5, 130.2, 128.6, 74.2, 69.9, 68.2, 54.7, 18.1; IR (neat) 3440, 1764, 1689.

[2*S*-(2 α ,3 β ,4 α ,4 α ,7 α)]-Hexahydro-4-hydroxy-3-iodo-2-(1*E*-propenyl)-5H-furo[3,4-*b*]pyran-5-one (14). Dry bis(*sym*-collidine)silver(I) hexafluorophosphate (375 mg, 0.81 mmol) was slurried in dry CH_2Cl_2 (5 mL) with vigorous stirring and iodine (154 mg, 0.61 mmol) was added in one portion and the solution was stirred for 5 min. A yellow precipitate was produced instantly. Diene diol **9a** (100 mg, 0.51 mmol) in dry CH_2Cl_2 (1 mL) was added and the resulting mixture was stirred at rt for 1.5 h and filtered through Celite. The filtrate was washed with 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution, saturated aqueous NaHCO_3 solution, dried (Na_2SO_4), and concentrated to give 160 mg (91%) of crude **14** as a yellow oil. Flash chromatography on silica gel (4:1 hexanes/EtOAc) gave 61 mg (37%) of **14** as a pale yellow solid, followed by 74 mg (45%) of **[2*S*-(2 α ,3 β ,4 α ,4 α ,7 α)]-hexahydro-4-hydroxy-3-iodo-2-(1*E*-propenyl)-5H-furo[3,4-*b*]pyran-5-one (18).**

Isomerization of **14** to **18** could be minimized by chromatography on silica gel deactivated by storage in an open container for several months, which gave 80% of **14** and <5% of **18**. For sensitive compounds, silica gel was deactivated by addition of 5-10% water and stirring for 1 h on a rotary evaporator without vacuum.

Data for **14**: mp 124-125 °C; ^1H NMR 5.93 (dq, 1, $J = 15.3, 6.7$), 5.46 (ddq, 1, $J = 15.3, 7.9, 1.8$), 4.49 (dd, 1, $J = 7.9, 6.7, \text{H}_7$), 4.29 (dd, 1, $J = 10.4, 7.9, \text{H}_2$), 4.16 (ddd, 1, $J = 10.4, 9.8, 3.1, \text{H}_4$), 4.11 (dd, 1, $J = 10.0, 7.9, \text{H}_7$), 3.99 (ddd, 1, $J = 11.6, 10.0, 6.7, \text{H}_{7a}$), 3.63 (dd, 1, $J = 10.4, 9.8, \text{H}_3$), 3.29 (dd, 1, $J = 3.1, \text{OH}$), 2.41 (dd, 1, $J = 11.6, 10.4, \text{H}_{4a}$), 1.81 (dd, 3, $J = 6.7, 1.8$); ^{13}C NMR 170.4, 134.2, 127.6, 84.9, 74.4, 73.0, 68.8, 50.4, 38.5, 17.7; IR (KBr) 3505, 1785.

Data for **18**: ^1H NMR 5.83 (dq, 1, $J = 15.3, 6.1$), 5.44 (ddq, 1, $J = 15.3, 7.9, 1.8$), 4.491 (dd, 1, $J = 3.7, 3.7$, H_{7a}), 4.485 (d, 1, $J = 10.0$, OH), 4.42 (d, 1, $J = 10.4$, H_7), 4.32 (dd, 1, $J = 10.4, 3.7$, H_7), 4.15 (ddd, 1, $J = 10.4, 10.0, 6.7$, H_4), 3.95 (dd, 1, $J = 11.0, 7.9$, H_2), 3.70 (dd, 1, $J = 11.0, 10.4$, H_3), 3.07 (dd, 1, $J = 6.7, 3.7$, H_{4a}), 1.79 (dd, 3, $J = 6.1, 1.8$).

[2*S*-(2 α ,3 β ,4 β ,4 α ,7 α β)]-Hexahydro-4-hydroxy-3-iodo-2-(1*E*-propenyl)-5*H*-furo[3,4-*b*]pyran-5-one (16**)**. To a stirred solution of **12a** (62 mg, 0.31 mmol) in CH_3CN (3 mL) was added solid NaHCO_3 (85 mg, 1.01 mmol) at rt. The mixture was stirred for 10 min, cooled to 0 °C, and treated with I_2 (257 mg, 1.01 mmol). The resulting mixture was stirred for 2.5 h from 0 °C to rt and quenched with 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution. The mixture was saturated with NaCl and extracted several times with EtOAc. The combined extracts were washed with saturated aqueous NaHCO_3 solution, dried (Na_2SO_4), and concentrated to give a yellow oil. Flash chromatography on deactivated silica gel (6:1 hexanes/EtOAc) gave (71 mg, 70%) of **16**: mp 71-73 °C; ^1H NMR 5.89 (dq, 1, $J = 15.3, 6.7$), 5.39 (br dq, 1, $J = 15.3, 7.9$), 4.65 (br, 1, H_4), 4.60 (ddd, 1, $J = 11.6, 10.0, 7.0$, H_{7a}), 4.45 (dd, 1, $J = 7.9, 7.0$, H_7), 4.39 (dd, 1, $J = 10.4, 7.9$, H_2), 4.04 (br d, 1, $J = 10.4$, H_3), 4.03 (dd, 1, $J = 10.0, 7.9$, H_7), 2.80 (d, 1, $J = 2.4$, OH), 2.72 (br d, 1, $J = 11.6$, H_{4a}), 1.79 (br d, 3, $J = 6.7$); ^{13}C NMR 169.8, 134.0, 128.0, 79.1, 69.7, 69.0, 66.8, 48.9, 39.2, 17.7.

An identical reaction was concentrated (80 °C, 50 torr) to remove the CH_3CN after quenching with 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution. The aqueous layer was extracted with CH_2Cl_2 , which was washed with saturated aqueous NaHCO_3 solution, dried (Na_2SO_4), and concentrated to give a yellow oil. Flash chromatography on silica gel (6:1 hexanes/EtOAc) gave (74 mg, 73%) of **17** as colorless crystals: mp 89-92 °C; ^1H NMR 5.81 (dq, 1, $J = 15.3, 6.7$), 5.35 (ddq, 1, $J = 15.3, 7.9, 1.8$), 4.68 (dd, 1, $J = 3.9, 3.0$, H_{7a}), 4.57 (dd, 1, $J = 2.8, 2.4, 2.4$, H_4), 4.35 (d, 1, $J = 10.4$, H_7), 4.30 (dd, 1, $J = 10.4, 7.9$, H_2), 4.25 (dd, 1, $J = 10.4, 3.0$, H_7), 4.10 (dd, 1, $J = 10.4, 2.4$, H_3), 3.06 (dd, 1, $J = 3.9, 2.8$, H_{4a}), 2.54 (d, 1, $J = 2.4$, OH), 1.76 (dd, 3, $J = 6.7, 1.8$); ^{13}C NMR 173.7, 132.9, 129.1, 75.0, 72.8, 71.7, 67.3, 46.6, 39.1, 17.7; IR (KBr) 3456, 1768, 1677.

[2*S*-(2 α ,3 α ,7 α β)]-2,3,7,7a-Tetrahydro-3-hydroxy-2-(1*E*-propenyl)-5H-furo[3,4-*b*]pyran-5-one (21). To a solution of **14** (83 mg, 0.26 mmol) in dry CH₂Cl₂ (5 mL) was added Et₃N (2 mL). The resulting mixture was stirred at rt for 3 days, diluted with CH₂Cl₂ (125 mL), washed with 10% aqueous HCl, saturated aqueous NaHCO₃ solution, and brine, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (4:1 hexanes/EtOAc) gave **21** (45 mg, 87%) as a colorless oil: $[\alpha]_D^{20} +174$ (*c* 0.16, CHCl₃); ¹H NMR 6.93 (dd, 1, *J* = 3.7, 2.4, H₄), 5.94 (dq, 1, *J* = 15.3, 6.7), 5.71 (ddq, 1, *J* = 15.3, 6.1, 1.2), 4.77 (dddd, 1, *J* = 8.6, 8.6, 2.4, 2.4, H_{7a}), 4.65 (dd, 1, *J* = 8.6, 8.6, H₇), 4.09-4.12 (m, 2, H_{2,3}), 4.06 (dd, 1, *J* = 8.6, 8.6, H₇), 2.10 (d, 1, *J* = 7.9, OH), 1.81 (dd, 3, *J* = 6.7, 1.2); ¹³C NMR 167.1, 134.5, 131.9, 131.5, 125.5, 79.8, 73.1, 69.8, 64.0, 18.1; IR (neat) 3440, 1764, 1689; HRMS (CI/NH₃) calcd for C₁₀H₁₆NO₄ (MNH₄⁺) 214.1079, found 214.1084.

(3*R*,4*R*,5*S*)-Dihydro-4-hydroxy-3-(1*S*-hydroxyhexa-2*E*,4*E*-dienyl)-5-methylfuran-2-one (9b) and (3*R*,4*R*,5*S*)-Dihydro-4-hydroxy-3-(1*R*-hydroxyhexa-2*E*,4*E*-dienyl)-5-methylfuran-2-one (12b). Lithium diisopropylamide was prepared from diisopropylamine (292 μ L, 2.08 mmol) and *n*-BuLi (745 μ L, 2.79 M in hexane, 2.08 mmol) in THF (4 mL) at 0 °C. The solution was cooled to -23 °C and treated with **10b** (116 mg, 1 mmol) in THF (1 mL). The mixture was stirred for 15 min, cooled to -43 °C and treated with a 4:1 mixture of (2*E*,4*E*)- and (2*E*,4*Z*)-2,4-hexadienal (**11**) (110 μ L, 1 mmol). The mixture was stirred at -43 °C for 1 h and saturated aqueous NH₄Cl solution (1 mL) was added to quench the reaction. The resulting mixture was diluted with ether (80 mL), washed with brine, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (2:1 hexanes/EtOAc) gave **12b** (42 mg, 20%) as a colorless oil, followed by **9b** (103 mg, 49%) as a white solid. Both of these compounds are a 4:1 mixture of (2*E*,4*E*) and (2*E*,4*Z*) isomers. Flash chromatography of the mixture of **9b** isomers on 20% AgNO₃ on silica gel (2:1 hexanes/EtOAc) gave (2*E*,4*E*)-**9b** (80 mg, 38%). Similar chromatography of the mixture of **12b** isomers gave (2*E*,4*E*)-**12b** (30 mg, 14%).

Data for **9b**: ^1H NMR 6.32 (dd, 1, J = 15.3, 10.4), 6.07 (ddq, 1, J = 15.3, 10.4, 1.2), 5.79 (dq, 1, J = 15.3, 6.7), 5.67 (dd, 1, J = 15.3, 7.3), 4.53 (ddd, 1, J = 7.3, 6.7, 3.1), 4.26 (dq, 1, J = 7.9, 6.1), 3.98 (ddd, 1, J = 8.5, 7.9, 4.3), 3.18 (d, 1, J = 3.1, OH), 2.85 (dd, 1, J = 8.5, 6.7), 2.46 (d, 1, J = 4.3, OH), 1.77 (dd, 3, J = 6.7, 1.2), 1.46 (d, 3, J = 6.1); ^{13}C NMR 174.6, 133.7, 132.0, 130.1, 127.7, 80.1, 75.2, 71.3, 54.3, 18.1, 18.0; IR (KBr) 3401, 1761, 1662; HRMS (CI/NH₃) calcd for C₁₁H₂₀NO₄ (MNH₄⁺) 230.1392, found 230.1395.

Data for **12b**: ^1H NMR 6.37 (dd, 1, J = 15.3, 10.4), 6.07 (dd, 1, J = 15.3, 10.4), 5.78 (dq, 1, J = 15.3, 6.1), 5.69 (dd, 1, J = 15.3, 6.1), 4.73 (ddd, 1, J = 6.1, 4.3, 3.7), 4.27 (dq, 1, J = 8.5, 6.1), 4.20 (ddd, 1, J = 8.5, 7.9, 4.3), 2.79 (dd, 1, J = 7.9, 3.7), 2.74 (d, 1, J = 4.3, OH), 2.64 (d, 1, J = 4.3, OH), 1.77 (d, 3, J = 6.1), 1.46 (d, 3, J = 6.1); ^{13}C NMR 174.4, 132.1, 131.4, 130.3, 128.8, 80.1, 74.3, 69.1, 55.0, 18.1, 18.1; IR (KBr) 3430, 1759, 1661.

[2*R*-(2 α ,3 β ,4 α ,4 α ,7 β ,7 α)]-Hexahydro-4-hydroxy-3-iodo-7-methyl-2-(1*E*-propenyl)-5*H*-furo[3,4-*b*]pyran-5-one (8b). Dry bis(*sym*-collidine)silver(I) hexafluorophosphate (238 mg, 0.51 mmol) was slurried in dry CH₂Cl₂ (3 mL) with vigorous stirring and iodine (97 mg, 0.38 mmol) was added in one portion and the solution was stirred for 5 min. A yellow precipitate was produced instantly. Diene diol **9b** (68 mg, 0.32 mmol) in dry CH₂Cl₂ (1 mL) was added and the resulting mixture was stirred at rt for 1.5 h and filtered through Celite. The filtrate was washed with 10% aqueous Na₂S₂O₃ solution, saturated aqueous NaHCO₃ solution, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (6:1 hexanes/EtOAc) gave **8b** (95mg, 88%) as a pale yellow solid: ^1H NMR 5.92 (dq, 1, J = 15.3, 6.7), 5.45 (ddq, 1, J = 15.3, 7.9, 1.2), 4.45 (dq, 1, J = 8.6, 6.1, H₇), 4.25 (dd, 1, J = 11.0, 7.9, H₂), 4.13 (ddd, 1, J = 10.4, 9.8, 2.4, H₄), 3.59 (dd, 1, J = 11.0, 9.8, H₃), 3.48 (dd, 1, J = 11.6, 8.6, H_{7a}), 3.07 (d, 1, J = 2.4, OH), 2.47 (dd, 1, J = 11.6, 10.4, H_{4a}), 1.80 (dd, 3, J = 6.7, 1.2), 1.51 (d, 3, J = 6.1); ^{13}C NMR 169.9, 134.2, 127.6, 84.9, 80.6, 78.3, 73.2, 51.6, 38.6, 17.7, 17.7; IR (KBr) 3469, 1784.

[2*R*-(2 α ,3 α ,7 β ,7 α)]-2,3,7,7*a*-Tetrahydro-3-hydroxy-7-methyl-2-(1*E*-propenyl)-5*H*-furo[3,4-*b*]pyran-5-one {(-)-TAN 2483A, **5}.** To a solution of **8b** (95 mg, 0.28mmol) in dry

CH₂Cl₂ (3 mL) was added Et₃N (2 mL). The resulting mixture was stirred at rt for three days and diluted with CH₂Cl₂ (80 mL), washed with 10% aqueous HCl, saturated aqueous NaHCO₃ solution, brine, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (4:1 hexanes/EtOAc) gave **5** (47 mg, 79%) as a colorless oil: $[\alpha]_D^{22}$ -236 (*c* 1.20, CHCl₃) {lit.⁴ $[\alpha]_D^{23}$ -293 (*c* 0.59, CHCl₃)}; ¹H NMR 6.88 (dd, 1, *J* = 3.7, 2.4, H₄), 5.94 (dq, 1, *J* = 15.3, 7.0), 5.70 (ddq, 1, *J* = 15.3, 6.1, 1.8), 4.34 (dq, 1, *J* = 7.3, 6.1, H₇), 4.25 (ddd, 1, *J* = 7.3, 2.4, 2.4, H_{7a}), 4.04-4.11 (m, 2, H_{2,3}), 1.78 (br d, 3, *J* = 7.0), 1.56 (d, 3, *J* = 6.1); ¹³C NMR 166.6, 133.4, 133.4, 131.3, 125.6, 79.9, 79.7, 79.0, 64.1, 18.8, 18.1; IR (neat) 3436, 1773, 1642; HRMS (CI/NH₃) calcd for C₁₁H₁₈NO₄ (MNH₄⁺) 228.1236, found 228.1233. The spectral data are identical to those of the natural product.⁴

2-(*tert*-Butyldiphenylsilyloxy)-3-pentenitrile (22). To a stirred solution of *trans*-2-butenal (2.8 g, 40 mmol) in ether (6 mL) at -10 °C was added a pre-cooled (-10 °C) solution of NaCN (1.96 g, 40 mmol) in H₂O (5 mL) over 3 min. A solution of HCl [36% HCl (2 mL) + H₂O (2 mL)] was added dropwise over 2 h at -10 °C. The mixture was stirred at rt for 3 h and the ether layer was separated, washed with water, dried (Na₂SO₄), and concentrated to give a yellow oil. Without further purification, the crude cyanohydrin was added to a solution of imidazole (3.78 g, 56 mmol) and *tert*-butyldiphenylsilyl chloride (7.2 mL, 28 mmol) in dry DMF (75 mL) at 0 °C. The resulting mixture was stirred overnight from 0 °C to rt and poured into 80 mL of H₂O, which was extracted with ether, which was washed with brine and concentrated to give a yellow oil. Flash chromatography on silica gel (40:1 hexanes/ether) gave **22**¹⁴ (4.69 g, 34%) as a colorless oil.

Methyl 4-(*tert*-Butyldiphenylsilyloxy)-3-oxo-5-heptenoate (23). Powdered zinc was activated by washing sequentially with 3 M HCl, water, EtOH, and ether and drying under reduced pressure.¹⁵ To a solution of activated zinc dust (1.06 g, 16.22 mmol) in dry THF (15 mL) was added TMSCl (189 μL, 1.49 mmol). The solution was stirred for 20 min, treated with **22** (1.93 g, 5.76 mmol), and the mixture heated to reflux. Methyl bromoacetate (1.69 mL, 17.90 mmol) was added dropwise over 50 min and heating was continued for 70 min. The mixture was

cooled to 5 °C, 3 M HCl (9 mL) was added and the resulting solution was stirred at rt for 2 h. The mixture was poured into saturated aqueous NaHCO₃ solution (50 mL) forming an emulsion that was broken by the addition of water (50 mL). The aqueous phase was extracted with EtOAc (5 × 80 mL), and the combined organic layers were dried (Na₂SO₄) and concentrated to give a yellow oil. Flash chromatography on silica gel (20:1 hexanes/ether) gave **23** (2.03 g, 86%) as an 87:13 keto/enol mixture: ¹H NMR (keto) 7.59-7.62 (m, 4), 7.36-7.44 (m, 6), 5.62 (ddq, 1, *J* = 15.3, 6.7, 1.2), 5.35 (ddq, 1, *J* = 15.3, 6.4, 1.8), 4.58 (br d, 1, *J* = 6.4), 3.67 (s, 3), 3.57 (s, 2), 1.59 (ddd, 3, *J* = 6.7, 1.8, 1.2), 1.10 (s, 9); (enol) 11.8 (s, 1, OH), 5.44 (s, 1); ¹³C NMR (keto) 202.6, 167.7, 135.8 (2 C), 135.7 (2 C), 132.9, 132.6, 130.9, 130.1, 129.9, 127.8 (2C), 127.6 (2C), 126.9, 80.5, 52.2, 43.9, 26.9 (3 C), 19.3, 17.8; IR (neat) 2955, 1755, 1725; HRMS (DCI/NH₃) calcd for C₂₄H₃₄NO₄Si (MNH₄⁺) 428.2257, found 428.2265.

Methyl 4-(*tert*-Butyldiphenylsilyloxy)-3-hydroxy-5-heptenoate (24). To a stirred solution of **23** (1 g, 2.43 mmol) in MeOH (10 mL) at -15 °C was added NaBH₄ (111 mg, 2.92 mmol) in portions. The solution was stirred for 5 min and 10% aqueous HCl was added to quench the reaction. After concentration to remove the MeOH, the aqueous phase was extracted with EtOAc (3 × 80 mL), which was washed with saturated aqueous NaHCO₃ solution, brine, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (4:1 hexanes/ether) gave (970 mg, 97 %) of an inseparable 5:1 mixture of **24a** and **24b**.

Partial data for **24a** were determined from the mixture: ¹H NMR 3.656 (s, 3), 2.65 (d, 1, *J* = 3.7, OH); 2.48 (dd, 1, *J* = 15.9, 4.3), 2.45 (dd, 1, *J* = 15.9, 7.9).

Partial data for **24b** were determined from the mixture: ¹H NMR 3.663 (s, 3), 2.78 (d, 1, *J* = 4.3, OH); 2.52 (dd, 1, *J* = 15.2, 3.7), 2.36 (dd, 1, *J* = 15.2, 8.5).

***trans*-Dihydro-4-hydroxy-5-(1*E*-propenyl)-furan-2-one (10c) and *cis*-Dihydro-4-hydroxy-5-(1*E*-propenyl)-furan-2-one (25).** To a cooled solution (5 °C) of the 5:1 mixture of **24a** and **24b** (890 mg, 2.16 mmol) in THF (20 mL) was added TBAF (6.8 mL, 0.7 M in CH₃CN, 4.76 mmol) dropwise. The reaction was stirred for 48 h at rt and treated with 10% aqueous HCl (2 mL). The solution was stirred for 1 h. Ethyl acetate and solid NaCl were added. The layers

were separated and the organic layer was washed with saturated aqueous NaHCO₃ solution, brine, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (1:1 hexanes/EtOAc) gave **10c** (193mg, 63%) as a colorless oil, followed by **25** (40 mg, 13%) also as a colorless oil.

Data for **10c**: ¹H NMR 5.88 (dq, 1, *J* = 15.3, 6.7), 5.46 (dd, 1, *J* = 15.3, 6.7), 4.77 (dd, 1, *J* = 6.7, 1.8), 4.33 (m, 1), 2.89 (br, 1, OH), 2.81 (dd, 1, *J* = 17.7, 6.7), 2.51 (dd, 1, *J* = 17.7, 4.3), 1.75 (d, 3, *J* = 6.7); ¹³C NMR 175.4, 131.2, 125.7, 87.7, 72.1, 37.0, 17.8; IR (neat) 3432, 1778, 1672; HRMS (CI/NH₃) calcd for C₇H₁₄NO₃ (MNH₄⁺) 160.0974, found 160.0969.

Data for **25**: ¹H NMR 6.01 (dq, 1, *J* = 15.3, 6.7), 5.63 (ddq, 1, *J* = 15.3, 6.7, 1.8), 4.86 (dd, 1, *J* = 6.7, 3.7), 4.48 (m, 1), 2.78 (dd, 1, *J* = 17.7, 5.7), 2.62 (dd, 1, *J* = 17.7, 1.8), 2.12 (d, 1, *J* = 3.1, OH), 1.82 (br d, 3, *J* = 6.7); ¹³C NMR 175.7, 133.6, 122.8, 84.9, 69.7, 38.7, 18.0; IR (neat) 3432, 1765.

(3*R,4*R*,5*S*)-Dihydro-4-hydroxy-3-(1*S*-hydroxyhexa-2*E*,4*E*-dienyl)-5-(1*E*-propenyl)-furan-2-one (9c) and (3*R**,4*R*,5*S*)-Dihydro-4-hydroxy-3-(1*R*-hydroxyhexa-2*E*,4*E*-dienyl)-5-(1*E*-propenyl)-furan-2-one (12c).** Lithium diisopropylamide was prepared from diisopropylamine (493 μL, 3.52 mmol) and *n*-BuLi (1.41 mL, 2.5 M in hexane, 3.52 mmol) in THF (10 mL) at 0 °C. This solution was cooled to -42 °C and treated with **10c** (200 mg, 1.41 mmol) in THF (1 mL). The solution was stirred for 15 min and a 4:1 mixture of (2*E*,4*E*)- and (2*E*,4*Z*)-2,4-hexadienal (156 μL, 1.42 mmol) was added. The mixture was stirred at -42 °C for 1 h and saturated aqueous NH₄Cl solution (1 mL) was added to quench the reaction. The resulting mixture was diluted with ether (125 mL), washed with brine, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (1:1 hexanes/ether) gave **12c** (90 mg, 27%) followed by **9c** (188 mg, 56%). Both of these compounds are a 4:1 mixture of (2*E*,4*E*) and (2*E*,4*Z*) isomers. Flash chromatography of the mixture of **9c** isomers on 20% AgNO₃ on silica gel (1:1 hexanes/EtOAc) gave (2*E*,4*E*)-**9c** (147 mg, 44%) as a white solid. Similar chromatography of the mixture of **12c** isomers gave (2*E*,4*E*)-**12c** as a white solid (71 mg, 21%).

Data for **9c**: mp 83-84 °C; ^1H NMR 6.32 (dd, 1, $J = 15.3, 11.0$), 6.07 (ddq, 1, $J = 15.3, 11.0, 1.8$), 5.97 (dq, 1, $J = 15.3, 6.7$), 5.79 (dq, 1, $J = 15.3, 6.7$), 5.67 (dd, 1, $J = 15.3, 7.3$), 5.49 (ddq, 1, $J = 15.3, 6.9, 1.8$), 4.49-4.53 (m, 2), 4.08 (ddd, 1, $J = 11.6, 9.2, 3.7$), 3.11 (d, 1, $J = 3.1, \text{OH}$), 2.84 (dd, 1, $J = 9.2, 6.7$), 2.34 (d, 1, $J = 3.7, \text{OH}$), 1.77 (dd, 6, $J = 6.7, 1.8$); ^{13}C NMR 174.2, 133.8, 133.6, 132.2, 130.1, 127.7, 125.9, 84.1, 74.1, 71.6, 53.6, 18.2, 17.9; IR (KBr) 3397, 1733, 1672; HRMS (CI/NH₃) calcd for C₁₃H₂₂NO₄ (MNH₄⁺) 256.1549, found 256.155269.

Data for **12c**: mp 95-98 °C; ^1H NMR 6.36 (dd, 1, $J = 15.3, 10.4$), 6.08 (ddq, 1, $J = 15.3, 10.4, 1.8$), 5.96 (dq, 1, $J = 15.3, 6.7$), 5.77 (dq, 1, $J = 15.3, 6.7$), 5.71 (dd, 1, $J = 15.3, 6.1$), 5.52 (ddq, 1, $J = 15.3, 7.9, 1.8$), 4.74 (ddd, 1, $J = 6.1, 4.3, 3.7$), 4.49 (dd, 1, $J = 7.9, 7.9$), 4.31 (ddd, 1, $J = 10.4, 7.9, 4.3$), 2.82 (d, 1, $J = 3.7, \text{OH}$), 2.80 (d, 1, $J = 4.3, \text{OH}$), 2.46 (dd, 1, $J = 10.4, 4.3$), 1.77 (br d, 6, $J = 6.7$); ^{13}C NMR 173.9, 133.4, 132.2, 131.4, 130.2, 128.6, 126.2, 84.3, 73.1, 69.2, 54.2, 18.1, 17.9; IR (KBr) 3337, 1767, 1676.

(2 α ,3 β ,4 α ,4 α ,7 β ,7 α)-Hexahydro-4-hydroxy-3-iodo-2,7-bis-(1*E*-propenyl)-5H-furo[3,4-*b*]pyran-5-one (8c). Dry bis(*sym*-collidine)silver(I) hexafluorophosphate (255 mg, 0.55 mmol) was slurried in dry CH₂Cl₂ (3 mL) with vigorous stirring and iodine (104 mg, 0.41 mmol) was added in one portion forming a yellow precipitate instantly. The solution was stirred for 5 min and diene diol **9c** (81 mg, 0.34 mmol) in dry CH₂Cl₂ (2 mL) was added. The resulting mixture was stirred at rt for 2 h and filtered through celite. The filtrate was washed with 10% aqueous Na₂S₂O₃ solution, saturated aqueous NaHCO₃ solution, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (3:1 hexanes/ether) gave **8c** (118 mg, 95%) as a pale yellow solid: mp 125-127 °C; ^1H NMR 6.01 (dq, 1, $J = 15.3, 6.7$), 5.90 (dq, 1, $J = 15.3, 6.7$), 5.49 (ddq, 1, $J = 15.3, 7.9, 1.2$), 5.43 (ddq, 1, $J = 15.3, 7.9, 1.2$), 4.71 (dd, 1, $J = 8.6, 7.9, \text{H}_7$), 4.24 (dd, 1, $J = 10.4, 7.9, \text{H}_2$), 4.14 (dd, 1, $J = 10.4, 9.8, \text{H}_4$), 3.61 (dd, 1, $J = 11.6, 8.6, \text{H}_{7a}$), 3.60 (dd, 1, $J = 10.4, 9.8, \text{H}_3$), 3.17 (br, 1, OH), 2.48 (dd, 1, $J = 11.6, 10.4, \text{H}_{4a}$), 1.79 (dd, 3, $J = 6.7, 1.2$), 1.78 (dd, 3, $J = 6.7, 1.2$); ^{13}C NMR 169.7, 135.0, 134.2, 127.5, 124.9, 84.9, 82.3, 79.2, 73.1, 51.3, 38.6 18.0, 17.7; IR (KBr) 3449, 1768, 1677.

(2 α ,3 α ,7 β ,7a β)-2,3,7,7a-Tetrahydro-3-hydroxy-2,7-bis-(1*E*-propenyl)-5H-furo[3,4-*b*]pyran-5-one {(\pm)-Waol A, **6}. To a solution of **8c** (90 mg, 0.25 mmol) in dry CH₂Cl₂ (10 mL) was added Et₃N (2 mL). The resulting mixture was stirred at reflux overnight, diluted with CH₂Cl₂ (125 mL), washed with 10% aqueous HCl, saturated aqueous NaHCO₃ solution and brine, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (1:1 hexanes/ether) gave **6** (57 mg, 98%) as a colorless oil: ¹H NMR 6.89 (dd, 1, *J* = 3.7, 2.4, H₄); 6.01 (dq, 1, *J* = 15.3, 6.7), 5.92 (dq, 1, *J* = 15.3, 6.7), 5.71 (ddq, 1, *J* = 15.3, 6.7, 1.2), 5.61 (ddq, 1, *J* = 15.3, 7.9, 1.2), 4.60 (dd, 1, *J* = 7.9, 7.9, H₇), 4.38 (ddd, 1, *J* = 7.9, 2.4, 1.8, H_{7a}), 4.04-4.08 (m, 2, H_{2,3}), 2.07 (br d, 1, *J* = 7.9, OH), 1.79 (dd, 6, *J* = 6.7, 1.2); ¹³C NMR 166.4, 134.0, 133.6, 132.9, 131.3, 125.9, 125.7, 82.9, 79.8, 78.5, 64.1, 18.1, 17.9; IR (neat) 3440, 1762, 1674; HRMS (CI/NH₃) calcd for C₁₃H₂₀NO₄ (MNH₄⁺) 254.1392, found 254.1381. The spectral data are identical to those of natural waol A.¹**

Methyl (1'*R,2*S*,5*S*,6*S*)-5,6-Dihydro-5-hydroxy-2-(1-hydroxy-2*E*-butenyl)-6-(1*E*-propenyl)-2H-pyran-3-carboxylate {(\pm)-Waol B, **26**} and (2 α ,3 α ,4 β ,4a β ,7 β ,7a β)-Hexahydro-3-hydroxy-4-methoxy-2,7-bis-(1*E*-propenyl)-5H-furo[3,4-*b*]pyran-5-one (**27**). A solution of **6** (20 mg, 0.08 mmol) in 5 mL of 1:1 MeOH/H₂O containing 142 mg of KOH was stirred for 1 h. The MeOH was removed by concentration and the resulting aqueous solution was acidified with 0.5 M HCl to pH 3 and extracted with Et₂O (3 \times 15 mL). The combined extracts were washed with H₂O and dried (Na₂SO₄). A solution of diazomethane in ether was added dropwise to the Et₂O solution at 0 °C. Concentration afforded an oil that was purified by flash chromatography on silica gel (3:1 hexanes/EtOAc) to give **27** (10.6 mg, 47%) as a colorless oil, followed by **26** (8.6 mg, 38%) as a colorless oil.**

Data for **26**: ¹H NMR 7.13 (dd, 1, *J* = 6.4, 2.0, H₄), 5.84 (dq, 1, *J* = 15.3, 6.7), 5.62-5.71 (m, 2), 5.44 (ddq, 1, 15.3, 6.7, 1.8), 4.76 (br s, 1), 4.59-4.63 (m, 1), 3.91-3.97 (m, 2), 3.76 (s, 3), 2.55 (d, 1, *J* = 8.5, OH), 1.90 (d, 1, *J* = 10.4, OH), 1.77 (d, 3, *J* = 6.7), 1.68 (dd, 3, *J* = 6.7, 1.2); ¹³C NMR 165.7, 137.9, 132.7, 130.3, 128.9, 128.5, 126.7, 77.2, 76.8, 72.7, 64.3, 52.0, 18.1, 17.8;

IR (neat) 3415, 1717; HRMS (CI/NH₃) calcd for C₁₄H₂₄NO₅ (MNH₄⁺) 286.1654, found 286.1656. The spectral data are identical to those of natural waol B.²

Data for **27**: ¹H NMR 5.81-5.94 (m, 2), 5.54 (ddq, 1, *J* = 15.3, 6.7, 1.8), 5.42 (ddq, 1, *J* = 15.3, 5.5, 1.8), 4.98 (d, 1, *J* = 5.5, H₇), 4.28 (d, 1, *J* = 4.9, H_{7a}), 4.16 (dd, 1, *J* = 6.7, 1.2, H₂), 3.99 (dd, 1, *J* = 2.4, 1.8, H₄), 3.65 (dd, 1, *J* = 4.8, 2.4, H₃), 3.47 (s, 3), 2.74 (dd, 1, *J* = 4.9, 1.8, H_{4a}), 1.83 (d, 1, *J* = 4.8, OH), 1.72-1.76 (m, 6); ¹³C NMR 174.4, 130.2, 130.0, 126.7, 124.4, 84.2, 76.0, 75.6, 72.8, 66.8, 57.9, 39.9, 18.0, 17.8; IR (neat) 3477, 1770; HRMS (CI/NH₃) calcd for C₁₄H₂₄NO₅ (MNH₄⁺) 286.1654, found 286.1656.

(3*R,4*R*,5*R*)-Dihydro-4-hydroxy-3-(1*S*-hydroxyhexa-2*E*,4*E*-dienyl)-5-methylfuran-2-one (29) and (3*R**,4*R*,5*R*)-Dihydro-4-hydroxy-3-(1*R*-hydroxyhexa-2*E*,4*E*-dienyl)-5-methylfuran-2-one (30).** Lithium diisopropylamide was prepared from diisopropylamine (679 μL, 4.84 mmol) and *n*-BuLi (1.73 mL, 2.79 M in hexane, 4.84 mmol) in THF (8 mL) at 0 °C. The solution was cooled to -23 °C and treated with **28** (270 mg, 2.33 mmol) in THF (1 mL). The mixture was stirred for 15 min, cooled to -43 °C, and treated with a 4:1 mixture of (2*E*,4*E*)- and (2*E*,4*Z*)-2,4-hexadienal (0.11 mL, 1 mmol). The mixture was stirred at -43 °C for 1.2 h and saturated aqueous NH₄Cl solution (1 mL) was added to quench the reaction. The resulting mixture was diluted with ether (150 mL), washed with brine, dried (Na₂SO₄), and concentrated to give a yellow oil. Flash chromatography on silica gel (2:1 hexanes/EtOAc) gave **30** (193 mg, 39%) as a colorless oil, followed by **29** (188 mg, 38%) as a white solid. Both of these compounds are a 4:1 mixture of (2*E*,4*E*) and (2*E*,4*Z*) isomers. Flash chromatography of the mixture of **29** isomers on 20% AgNO₃ on silica gel (2:1 hexanes/EtOAc) gave (2*E*,4*E*)-**29** (143 mg, 29%). Similar chromatography of the mixture of **30** isomers gave (2*E*,4*E*)-**30** (150 mg, 30%).

Data for **29**: ¹H NMR 6.29 (dd, 1, *J* = 15.3, 10.4), 6.06 (ddq, 1, *J* = 15.3, 10.4, 1.3), 5.78 (dq, 1, *J* = 15.3, 6.7), 5.67 (dd, 1, *J* = 15.3, 7.3), 4.69 (dq, 1, *J* = 6.7, 6.7), 4.53 (dd, 1, *J* = 7.3, 6.5), 4.45 (dd, 1, *J* = 6.7, 6.7), 3.10 (br, 1, OH), 2.81 (dd, 1, *J* = 6.7, 6.5), 1.96 (br, 1, OH), 1.78

(dd, 3, $J = 6.7, 1.3$), 1.38 (br d, 3, $J = 6.7$); ^{13}C NMR 175.4, 133.6, 132.1, 130.1, 127.8, 78.8, 71.5, 70.7, 53.7, 18.1, 14.2.

Data for **30**: ^1H NMR 6.31 (dd, 1, $J = 15.3, 10.4$), 6.06 (ddq, 1, $J = 15.3, 10.4, 1.2$), 5.76 (dq, 1, $J = 15.3, 6.7$), 5.64 (dd, 1, $J = 15.3, 6.1$), 4.65-4.73 (m, 2), 4.50 (dd, 1, $J = 6.1, 4.3$), 3.28 (br, 2, OH), 2.71 (dd, 1, $J = 4.3, 3.7$), 1.77 (br d, 3, $J = 6.7$), 1.36 (d, 3, $J = 6.1$); ^{13}C NMR 177.0, 132.2, 131.2, 130.3, 128.9, 80.1, 70.2, 69.7, 55.2, 18.0, 14.0.

(2 α ,3 β ,4 α ,4 α ,7 α ,7 $\alpha\beta$)-Hexahydro-4-hydroxy-3-iodo-7-methyl-2-(1*E*-propenyl)-5H-furo[3,4-*b*]pyran-5-one (31). Dry bis(*sym*-collidine)silver(I) hexafluorophosphate (232 mg, 0.50 mmol) was slurried in dry CH_2Cl_2 (2 mL) with vigorous stirring and iodine (94 mg, 0.37 mmol) was added in one portion and the solution was stirred for 5 min. A yellow precipitate was produced instantly. Diene diol **29** (66 mg, 0.32 mmol) in dry CH_2Cl_2 (1 mL) was added. The resulting mixture was stirred at rt for 1.5 h and filtered through Celite. The filtrate was washed with 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution, saturated aqueous NaHCO_3 solution, dried (Na_2SO_4), and concentrated to give a yellow oil. Flash chromatography on silica gel (6:1 hexanes/EtOAc) gave **31** (97 mg, 92%) as a pale yellow solid: mp 85-89 °C; ^1H NMR 5.91 (dq, 1, $J = 15.3, 6.7$), 5.47 (ddq, 1, $J = 15.3, 7.9, 1.2$), 4.81 (dq, 1, $J = 7.3, 6.7, \text{H}_7$), 4.27 (dd, 1, $J = 11.0, 7.9, \text{H}_2$), 4.14 (ddd, 1, $J = 9.8, 9.8, 1.8, \text{H}_4$), 4.00 (dd, 1, $J = 12.2, 7.3, \text{H}_{7a}$), 3.58 (dd, 1, $J = 11.0, 9.8, \text{H}_3$), 3.24 (d, 1, $J = 1.8, \text{OH}$), 2.53 (dd, 1, $J = 12.2, 9.8, \text{H}_{4a}$), 1.80 (dd, 3, $J = 6.7, 1.2$), 1.41 (d, 3, $J = 6.7$); ^{13}C NMR 170.3, 133.8, 127.7, 84.9, 76.2, 75.6, 73.6, 46.6, 38.7, 17.7, 13.5.

(2 α ,3 α ,7 α ,7 $\alpha\beta$)-2,3,7,7a-Tetrahydro-3-hydroxy-7-methyl-2-(1*E*-propenyl)-5H-furo[3,4-*b*]pyran-5-one (32). To a solution of **31** (83 mg, 0.25 mmol) in dry CH_2Cl_2 (3 mL) was added Et_3N (2 mL). The resulting mixture was stirred at reflux for 3 days, diluted with CH_2Cl_2 (80 mL), washed with 10% aqueous HCl, saturated aqueous NaHCO_3 solution, and brine, dried (Na_2SO_4), and concentrated to give a yellow oil. Flash chromatography on silica gel (4:1 hexanes/EtOAc) gave recovered **31** (51 mg, 61%), followed by **32** (16 mg, 32%) as a colorless oil.

In an improved procedure, DBN (25 μ L, 0.2 mmol) was added to a solution of **31** (14 mg, 0.04 mmol) in dry CH_2Cl_2 (1 mL). The solution was stirred at 0 $^\circ\text{C}$ for 1 h and quenched with water. The layers were separated and the water layer was extracted with CH_2Cl_2 . The combined organic layers were washed with 5% aqueous HCl, saturated aqueous NaHCO_3 solution, and brine, dried (Na_2SO_4), and concentrated to give a yellow oil. Flash chromatography on silica gel (4:1 hexanes/EtOAc) gave **32** (7.7 mg, 89%) as a colorless oil: ^1H NMR 6.98 (dd, 1, $J = 3.7, 2.4$, H_4), 5.94 (dq, 1, $J = 15.3, 6.7$), 5.71 (ddq, 1, $J = 15.3, 6.1, 1.2$), 4.91 (dq, 1, $J = 7.9, 6.7$, H_7), 4.75 (ddd, 1, $J = 7.9, 2.4, 2.4$, H_{7a}), 4.04-4.09 (m, 2, $\text{H}_{2,3}$), 1.79 (br d, 3, $J = 6.7$), 1.75 (d, 1, $J = 8.5$, OH), 1.27 (d, 3, $J = 6.7$); ^{13}C NMR 166.7, 134.9, 131.4, 131.2, 125.7, 79.4, 76.9, 74.7, 63.9, 18.1, 15.2; IR (neat) 3428, 1759, 1646; HRMS (CI/ NH_3) calcd for $\text{C}_{11}\text{H}_{18}\text{NO}_4$ (MNH_4^+) 228.1236, found 228.1240.